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To: <wvogl@samhsa.gov>
Date: 7/11/04 7:45PM
Subject: Docket # 04-7984 Comments

Dr. Vogl:

Please accept my attached comments to the DHHS/SAMHSA Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs (Docket Number 04-7984). I appreciate the opportunity to comment and thereby have a voice in the rulemaking process. Sincerely,

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The following comments are submitted to DHHS/SAMHSA Proposed Revisions to Mandatory Guidelines for Federal Workplace Drug Testing Programs (FR Doc. 04-7984)

General Comments:

The vast majority of regulated workplace drug testing is DOT-mandated drug testing, not drug testing of Federal employees. Many of the provisions in the HHS proposal will necessarily have to be incorporated into DOT workplace drug testing guidelines and ultimately into private sector workplace drug testing programs. The proposal as written relies too heavily on Federal agencies to perform certain critical functions (such as oversight and management of POCT programs). In DOT-mandated drug testing, there is no entity analogous to a Federal agency. Consequently, if this proposal were implemented for DOT-mandated drug testing, there is not sufficient oversight of the program to ensure reliable operation. For this reason I agree with Mr. Edgell's suggestion that the proposal should be withdrawn at this time and resubmitted as a unified DHHS-DOT "One Government" proposal that would apply to all Federal and DOT-mandated drug testing.

Although both GC-MS-MS and LC-MS-MS have been proposed as methods of choice for confirmatory testing for oral fluid and hair, the proposal includes no guidance or rules for use of those techniques. The well established criteria for chromatography, ion ratios, etc. in GC-MS will not directly apply to MS-MS techniques. Either the acceptance criteria should be stated in the proposal, or the proposal should state that the HHS contractor (NLCP?) will draw up the requirements. I would prefer to see more detail on MS/MS requirements in the actual proposal.

There are many other flaws in the proposal which must be addressed. Mr. Edgell has outlined many of them and offered the opinion that the proposal meets criteria for an Advance Notice of Proposed Rulemaking (ANPRM), but has too many holes to qualify as a Notice of Proposed Rulemaking (NPRM). I agree with that assessment and with the proposal that parts of the document could be reworked and republished as Advance Notices of Proposed Rulemaking. I will confine my comments to areas in which we have personal experience and/or strong opinions.

Subpart C – Drug & Validity Tests

To test for the amphetamine class, I do not think it should be required to do separate initial tests, one focused on amphetamine/methamphetamine and one focused on MDMA. Microgenics offers a single Amphetamine-Ecstasy initial test that works very well for amphetamine and methamphetamine at the current cutoffs, but also detects MDMA and Ecstasy-like compounds at similar concentrations. I suspect that Microgenics and others could produce suitable reagents to meet the new requirements and cutoffs. Many labs will probably offer a combined methamphetamine/amphetamine/MDMA/MDA/MDEA confirmatory test. It would be more efficient to do a single initial test for the

amphetamine class, and labs should be allowed to do that if reagents that meet the requirements are available.

Section 3.11

The proposed HHS NPRM requires validity testing for "one or more oxidizing adulterants." A laboratory can therefore meet the requirement either by doing a test for a single oxidant of its choice, a selection of multiple specific oxidants, or a general oxidant assay that detects a wide variety of oxidants. This is a problem for several reasons:

- Some laboratories will choose to meet this requirement by testing for only one oxidant at the lowest possible cost, and that would likely be nitrite. They'll meet the requirement, but they won't detect many adulterated specimens.
- Specimens tested at labs that test only for a single unpopular oxidant such as nitrite will have a greater chance of eluding adulterant detection than those tested at a lab that does a general oxidant assay.
- MROs will be continue to be confused about what adulterant tests and validity tests are being performed at each certified lab, necessitating extra phone calls between lab and MRO, extra comments on laboratory reports, etc.
- Employers and TPAs will be told by laboratory marketing reps that the lab is doing a "complete adulterant panel" no matter what oxidants the lab actually tests for. Most employers and TPAs won't know the difference. (This is happening now.)
- It will cause problems with submission of external blind specimens. For example, an agency or employer may submit an external blind specimen containing an adulterant (e.g., chromium VI) to a lab that tests only for nitrite. The lab will fail to detect chromium VI and therefore not report the specimen as "Invalid" or "Adulterated", resulting in a perception of an "error" by the testing laboratory. This type of scenario will result in needless rounds of "problem investigation" between labs, employers, NLCP, DOT, and DHHS.

Recommendation: All certified labs should be required, as part of every initial test, to do a general oxidant test that detects a wide variety of oxidizing adulterants. HHS and DOT should specify the requirements that must be met – that, is, what specific adulterants must be detected at specified cutoff levels -- for a general oxidant assay to be acceptable. This should not be an onerous requirement to implement. Several vendors offer reliable general oxidant assays right now. The benefit of this approach is that all certified labs will offer the same initial test – an immunoassay for the required drug classes, plus validity testing including pH, creatinine, SG, and general oxidants.

Oral Fluid

Of all of the alternative specimens, oral fluid offers the most promise as a way to improve upon and enhance workplace drug testing. In theory, oral fluid testing can deliver outcomes (positivity rates for selected drugs) that are comparable to those obtained with urine drug testing, and can do so utilizing a collection procedure that is faster, easier,

more dignified, and far less prone to the nagging problems of adulteration, substitution, and dilution that have threatened to undermine urine drug testing. Oral fluid would also address the significant problem of "shy bladder" syndrome which makes it difficult for individuals affected by paruresis to get fair treatment in urine drug testing programs. The published results by Ed Cone and colleagues in which 77,000 workplace oral fluid specimens tested over a one year period produced a very similar, and in some cases better, detection rate for tested drug classes compared to urine testing is a compelling finding. The results in that paper suggest that oral fluid could be used effectively in workplace drug testing. (See Cone et al., JAT, 26: 541-546, 2002).

However, HHS has raised some significant concerns, and the DHHS proposal as written negates almost all of the potential benefits of using oral fluid as a drug testing specimen. Here are the problems:

- HHS does not approve of using a collection device because it's concerned that stimulation of oral fluid flow will affect pH and possibly affect drug concentrations in oral fluid.
- HHS believes that a collection device does not produce a uniform volume of fluid in which to measure drug concentrations, thereby resulting in an unfair situation – that is, one donor's oral fluid specimen may not be the same volume as another's, and drug concentrations in the two fluids may not be directly comparable.
- HHS believes that there is not sufficient scientific evidence to differentiate between THC presence in oral fluid resulting from drug use vs. THC in oral fluid resulting from environmental contamination.

Because of these concerns, HHS has drafted a "crippled" proposal that has the following features:

- The donor would spit into a collection cup to produce 2.0 mL of fluid and the collector would quantitatively split the specimen into two portions. The procedure is disgusting and unsanitary, and I can't believe that collectors would actually do it.
- Oral fluid would not be effective in testing for marijuana (the number one abused drug), because a urine specimen would always have to be collected in addition to oral fluid, and a positive oral fluid initial test for THC would have to be confirmed by urine testing. No one will want to do that or pay for it, and the inevitable specimens that fail to confirm will require a lot of time and effort to investigate.

I believe that for oral fluid to be a viable alternative to urine for workplace drug testing, the following are needed:

1. The collections must be done using a collection device, not by having the donor spit into a cup.
2. Oral fluid must be capable of producing marijuana results that are forensically defensible without relying on testing a urine specimen collected at the same time.

Recommendations for Oral Fluid:

1. **HHS/DOT should examine the many sanitary convenient collection devices that are available today, decide on features that an approved collection device should possess, publish the requirements, and then publish a list of approved collection devices that meet criteria for acceptability.** If done properly, the device could provide a standardized way of collecting specimens that would address the concerns about specimen volume and drug concentrations in stimulated vs. unstimulated oral fluid.
2. **HHS and DOT should examine the scientific evidence and/or commission the studies needed to answer the question of whether it is possible to differentiate between THC in oral fluid resulting from drug use versus that resulting from environmental contamination.** I'm told that OraSure has unpublished data to help resolve the environmental contamination concern.

The oral fluid proposal in its current crippled state is impractical and could not be effectively used in workplace drug testing, so it's not worth proposing at this time and should be withdrawn. If both of the recommendations above are followed and the problems are resolved, then a revised more practical proposal could be submitted for consideration.

Subpart L – Point of Collection Test (POCT)

Excerpt from the preamble:

The value and utility of the POCT is that it provides quick, negative drug & validity test results and has the added benefit of not requiring a fixed facility, expensive test equipment, and highly trained testing personnel; moreover, POCTs could be run in low numbers, infrequently, and at any given location, as needed. These factors make it very difficult, if not impossible to use a laboratory "like" inspection and quality assurance process. The use of highly trained laboratory personnel provides no specific or added value to an oversight process, beyond the actual testing of samplePOCT devices. Further, the sheer potential number and diverse locations of sites where POCT devices might be used by choice, make large-scale, routine, or scheduled on-site inspections a logistic and budgeting nightmare.

Comments:

- It is a mistake to think that POCT can be easily done at any time anywhere without trained personnel and proper oversight. Each POCT event requires at a minimum a properly performed DOT collection, plus an onsite test, plus QC, plus documentation, plus recordkeeping, plus an immediate secure electronic report. I'm skeptical that this can be easily done, because DOT collections (without POCT) performed by supposedly "trained" collectors are frequently done improperly now. Our laboratory receives calls regularly from "trained" or "certified" specimen collectors who don't know how to do DOT-mandated collections, don't follow procedures, and just don't

care about doing it right. Sadly, neither do their supervisors, who often are not even involved in drug screen collections. Why would anyone think that adding a POC test plus reporting, recordkeeping, quality control, etc. to an already dismal collection situation would result in being able to do POC drug and validity tests without highly trained personnel, in low numbers, infrequently, and at any location, as needed? Bottom line: A POCT tester must receive training that's a lot better and more effective than what DOT collectors receive now.

- In addition to the training needed just to do the collection and do the test, somebody at that site has to ensure that the Guidelines are understood & followed, that standard operating procedures are in place & followed, that the integrity of the testing process is maintained, that QC is done & documented, that personnel are trained & training is documented, that specimens are handled in a forensically acceptable manner with chain of custody documentation, that reporting procedures are followed, that the testing site & records meet security requirements, etc, etc.
- In the current proposal, virtually all of the oversight functions for POCT fall on the federal agency rather than the POCT tester or a responsible person at the POCT site. If this proposal is adopted for use in DOT-mandated testing, there is no federal agency. I don't see how a POCT program will be managed properly if there is not someone analogous to a responsible person at each site.
- Although an employee of a Certified lab cannot perform DOT collections, the proposed Guidelines allow a POCT tester to also serve as the collector. This appears to be a contradiction. Of greater concern is that the POCT tester/collector may know the donor, or be bribed by a donor to record a negative result.
- There is no machine-generated documentation of donor results or QC for POCT testing. There is no real documentation to show that the POCT was even done.
- Presumably there will be a Federal POCT CCF. If a POCT is performed by someone other than the collector, the CCF will have to include a section for transfers of the specimen from the collector to the tester and from the tester to the courier (if needed), and possibly for POCT initial test results. The form is likely to be complex and prone to clerical errors, and it would be a good idea to propose a POCT CCF format for public comment.
- There will be problems if POCT sites send specimens to a Certified lab because of a positive POCT oxidant test, but the Certified lab only tests for nitrite. That is another reason why SVT requirements for POCT and for all certified labs should be the same.

Section 12.1 Goal of POCT

One of the stated goals of this section is to introduce POCT to provide an opportunity for testing of employees located in "remote areas of the country" or in "embassies in small foreign countries" – presumably because it is not possible to do a conventional laboratory-based test in those situations. Introducing POCT as a way to accomplish that goal makes no sense. A POCT requires a collector to do not only a standard DOT collection, but also to do an analytical test, report the result, maintain testing records, maintain QC materials and document a QC program, maintain training records, etc., and still send presumptive positive specimens to a certified lab for confirmatory testing. It seems that it would be

more difficult, not less, to establish and maintain a credible POCT program in a remote location or a small foreign country than it would be to simply do an acceptable DOT collection procedure and send the specimen to a lab. Specimen collection procedures are still the same & presumptive positives are still sent to a certified lab for confirmatory testing no matter how remote is the collection site.

The only situation in which it makes sense to do a POCT instead of a laboratory-based urine drug test is when it is critical to get an immediate negative result!

Section 12.2 What POCT Devices May Be Used?

The proposal requires that a POCT device effectively "determines the validity of a specimen, either as an integral function of the POCT device or as a set of compatible devices or procedures." Presumably this means that a POCT must perform to the same level and meet the same requirements as SVT conducted as part of a laboratory-based initial drug test. (This must be so, because later, in section 12.25, there's a requirement to provide a statistical summary report detailing the number of specimens that *screened* adulterated, substituted, and invalid.)

The preamble states that "non-instrumented specimen validity POCT for urine testing have been subjected to evaluations by independent investigators and were able to detect abnormal urine specimens." However, the references cited are all from work done three years ago, long before the current validity test requirements were in force. Is there any evidence that dipsticks or SVT tests integrated into POCT devices can reliably distinguish specimens with creatinine less than 2.0 mg/dL from those with creatinine greater than 2.0 mg/dL (the current cutoff for a substituted specimen), or can accurately detect the combinations of creatinine and SG that now define "invalid result"? I am not aware of any dipsticks or visually-read devices that can do that, or even approach that level of performance.

Unless there is reliable evidence that POCT can detect substituted, adulterated, or invalid specimens (using the current definitions for those reporting categories) in the same way as a laboratory-based urine drug test, the proposal to introduce POCT for federal workplace drug testing should be withdrawn.

Section 12.8 What Are the Responsibilities of a Federal Agency That Wishes to Conduct POCT?

The proposal requires that each agency that wants to do POCT must develop an SOP for testers, "periodically" inspect sites that do POCT, maintain tester training records, maintain PT records, provide semiannual statistics to DHHS, investigate all device and procedure failures, and so on. The problem here is that all of this responsibility falls on the federal agency, not the POCT tester and not the POCT site. In the real world, if this proposal ultimately applies to DOT-mandated testing (and it surely will), there is no federal agency. Who then will take care of all of these functions? It will have to be private

sector employers or collection sites themselves, and they can't do it. They do not have the financial resources, knowledge, or expertise to do so.

Although this proposal doesn't require it and indeed pooh-poohs the notion, we believe if you are going to do POCT at all, you need a trained & responsible individual at each POCT site who ensures that the Guidelines are understood & followed, that standard operating procedures are in place & followed, that the integrity of the testing process is maintained, that QC is done & documented, that personnel are trained & training is documented, that specimens are handled in a forensically acceptable manner with chain of custody documentation, that reporting procedures are followed, that the testing site & records meet security requirements, etc, etc.

Section 12.18 What Are the Requirements for Conducting a POCT?

The proposed collection procedure for conducting a POCT test – specifically, allowing the POCT tester to break the seal of Bottle A after the donor leaves the collection site -- is seriously flawed. Instead, the tester should do the POC test on the urine remaining in the collection cup.

Why? In the current DOT collection procedure, the donor observes his/her specimen being sealed with a tamper-evident seal bearing the unique Specimen Identification Number. Donor and collector participate in this process and initial and date the seals. The donor has assurance that the specimen will not be tampered with and will not be opened until it arrives at the secure certified laboratory that will test the specimen and produce the reportable result. In the proposed HHS procedure, there is no such assurance. The donor will observe his/her specimen being sealed, and then, as soon as he or she is out of view, the specimen seal will be broken, opening up a veritable Pandora's Box of potential errors, including:

- POCT tester tests more than one specimen at a time and mixes up the specimens being tested.
- POCT tester fails to properly reseal the Bottle A specimen or to initial and date the tamper-evident seal.
- POCT tester puts a dipstick directly into Bottle A to do a validity test.
- POCT tester fails to document chain of custody for taking the aliquot to do the analysis.

For the collection and POCT procedure to have any credibility, the sanctity of the sealed specimens must be preserved, just as it is in the current DOT collection procedure. In current DOT collections, we have observed that many supposedly "trained" collectors appear to have no idea what the purpose of the Specimen ID number is, or why the specimen must have a tamper-evident seal or how to apply one. Further, we are told by collectors that for non-DOT mandated POCT tests, they routinely have several specimen bottles open at a time and test them simultaneously. Why then would we expect them to follow the proposed procedure which requires them -- in an

unsupervised environment -- to break the seal, withdraw an aliquot, do the test, properly reseal the specimen, document all of that, and report the result, before going on to the next specimen? Keep in mind that for collectors and POCT testers, doing workplace drug testing is not their primary job. It's a sideline squeezed in among their other duties. Anything you do to increase the complexity of the collection/testing procedure increases the likelihood that they'll try to do too many things at once and will make errors. The DOT collection procedure is already in place and works if it's done properly. Don't deviate from it!

Recommendation: The POCT collector or tester must not be allowed to break the bottle A seal when the donor is not present. Instead, the collector/testor should do the test on the urine remaining in the collection cup, then discard that urine.

Section 12.19 What Are the Quality Control Requirements When Conducting POCTs?

For validity POCTs, it is proposed that each day testing is performed, at least one control that is normal for the specific validity test and one that is abnormal must be tested. **Instead, the Guidelines should spell out exactly what controls must be run and what results are acceptable, just as is done for laboratory testing. Otherwise, in the real world it will be left up to individual POCT testers to decide what controls to run and what passes as acceptable performance.** And, since collectors/testers will essentially be operating on the honor system, they may be easily tempted to report control results acceptable in order to avoid messy and time-consuming followup of failed QC.

It is proposed that at least one specimen out of every 10 specimens that test negative must be submitted to an HHS-certified laboratory as part of a quality assurance program. However, there are no details about the "quality assurance program." Who pays for the laboratory testing? What happens if the certified laboratory gets a confirmed positive on a specimen reported negative by the POCT tester? Where does the lab report that result? Who follows up and what action should be taken?

Section 12.20 What Action Must be Taken When a POCT Quality Control Sample Fails?

It is proposed that "..the failed quality control sample must be sent to an HHS-certified laboratory." What tests does the certified lab do on that QC sample – e.g., immunoassays for the stated drug classes, or quantitative GC-MS assays for each drug or analyte that the sample is supposed to contain? Where does the lab report these results, who follows up, what actions may be taken, and who pays for the lab testing?

The document refers to, but does not describe, a "quality assurance program" for POCT. The proposal should spell out exactly what will be done to assure someone that POCT is producing results that are equivalent to those that would be produced by a certified lab.

Section 12.22 How is a POCT Negative Result Reported?

The proposal requires that a negative result is reported directly to an MRO within 3 (average) working days after the POCT is conducted.

The current stipulation for laboratory-based testing is that a result should be reported within 5 working days – but everyone knows that the industry standard is: negative results are reported no later than the morning following collection of the specimen. That is, the real world requirement for a lab test is < 1 day.

There's no justifiable reason to do a POCT except when an immediate negative result is required. So, if you're going to do POCT at all, you should certainly report a result faster than an equivalent lab-based test would be reported, and at worst the report should be issued the same day of the analysis.

Recommendation: The requirement for reporting POCT results should be within 2 (average) hours after the specimen is collected for POCT, with *all* results transmitted to the MRO on the same day as the POCT test. If POCT is approved for regulated specimens, POCT testers and sites should be required to document that they are meeting this requirement.

Section 12.25 Statistical Summary Reports from POCT

The federal agency is supposed to submit to DHHS a semiannual statistical summary report for POCT tests that lists:

- The number screened positive for each drug
- Number screened adulterated
- Number screened substituted
- Number screened invalid
- Total number of QC samples tested, broken down into number of acceptable QCs and number of failed QCs.

As noted above, I don't believe that POCT sites will be able to do validity testing well enough to reliably categorize specimens as "adulterated," "substituted," or "invalid."

In the proposal the federal agency, not the POCT tester or POCT site, is required to prepare statistical summaries. In DOT-mandated testing, where there is no federal agency to provide oversight, who's going to do it? POCT sites and testers are almost certainly not going to be able to provide detailed statistical summary reports for each employer.

Also, regarding statistical summary reports: Right now, the onus is entirely on certified labs to produce semiannual statistical summaries – and it's a pain, but it's doable because all of the testing is done in certified labs, employers tend to utilize one lab, and labs have highly sophisticated LIMS systems and dedicated employees to meet the statistical report requirement. In the new proposal, a large employer could conceivably have POCT tests done at multiple sites (perhaps hundreds), plus testing at certified labs and IITFs. I foresee

the semiannual statistical summary requirement becoming a huge nightmare for all concerned, and frankly don't see how individual POCT sites can do it .

Recommendation: If the proposal to include POCT and IITFs is approved, the requirement for statistical summaries should transfer to the only entity that receives all of the results – the Medical Review Officer. MROs will hate me for proposing that, but I don't see any other way. Better yet: require employers to submit semiannual statistical summaries.

Subpart N Medical Review Officer (MRO)

Section 14.7(b) What Must an MRO Do When Reviewing a Urine Test Result?

This section would require the MRO to contact donors for all dilute specimens, and to attempt to determine whether there is a "legitimate medical explanation" for the dilute result. If there is not a legitimate medical explanation, recollection under direct observation would be required. How can the MRO possibly determine whether or not there is a legitimate explanation? The MRO is never going to have any real basis for deciding which specimens to recommend for recollection with direct observation. This requirement would significantly increase the burden on MROs, with no apparent benefit to anyone. **If the program feels strongly enough about dilute specimens, then attach a specific action or consequence (recollection with direct observation) to *all* dilute specimen results, with no donor interview required by the MRO. If dilute specimens aren't important enough to warrant such action, then do away with laboratory reporting of dilute specimens!** This may seem outrageous, because labs have reported "dilute" specimens since the beginning of the program, but think about it. There's never been a concrete action attached to a dilute result. Employers, MROs, and lab directors really don't know how to react to dilute results. (Probably the number one question asked by employers in private sector drug testing is "What should I do about Negative-Dilute results?" I have yet to come up with a satisfactory response.) Dr. Kammerer at CRL has advocated testing dilute specimens by GC-MS to the laboratory's LOQ for drugs that give a response higher than a negative control. That approach makes sense from a scientific standpoint, but has never gotten a very warm reception, presumably because it would require using a different cutoff for selected routine specimens. But asking the MRO to chase down every dilute specimen – which is clearly impossible for them to do -- is not the answer.